Structural and Functional Analysis of Mycobacterium Proteins
Implications for Drug Design
Felipe Marques Souza de Oliveira

Tuberculosis (TB) is a common and often deadly disease caused by the bacteria *Mycobacterium tuberculosis* (*M*. *tb*). This disease is responsible for approximately 1.6 million deaths every year. Although it is a very treatable disease, there has been an increase in drug resistance, which has led to the need for better drugs to be developed in the fight against tuberculosis. Therefore, several studies have been performed on the bacteria causing tuberculosis, and its development in the hopes of finding aspects which can be used in the development of such drugs.

In these studies several important facts about this bacterium have been discovered, such as its composition, and its cellular wall, which is a barrier that allows for the inflow of important nutrients and protects the cell. It is believed that the composition of this barrier is one of the key factors that lead to the drug resistance of this bacterium. Therefore, specific proteins that are responsible for the formation of this barrier have identified as hopeful targets for drug development. Two examples of these are the proteins referred to as IspD and IspH, which are members of a pathway that lead to other compounds responsible for the formation of the cell wall. Along with these two proteins other enzymes have been identified, such as ribonucleotide reductase, which is responsible for generating DNA, and Cysteinyl-tRNA synthetase, which is important in the organisms attempt to make proteins.

Therefore, studies of the mutated forms of these proteins were performed in order to allow for a better understanding of the structure and the interaction of these enzymes. Thus, crystallization experiments were done to understand the structure of these enzymes. These studies allow for the understanding of how to make drugs which are more efficient against tuberculosis as they will only affect those specific enzymes.

Although, the studies are on going we have successfully attained crystals for one of the proteins, the Cysteinyl-tRNA synthetase. We hope that in the near future we can determine the three dimensional structure of the protein so we can test compounds that can be used as future drugs against tuberculosis.